Medicinal and Bioorganic Chemistry of Nucleosides and Nucleotides

Foreword

Satoshi Shuto

*Faculty of Pharmaceutical Sciences, Hokkaido University;
Kita-12, Nishi-6, Kita-ku, Sapporo 060-0812, Japan.*

Nucleosides and nucleotides are of vital importance not only as components of ribo- and deoxyribonucleic acids in central dogma, but also as a wide variety of biofunctional molecules, such as chemical transmitters for receptors, second messengers in cellular signal transductions, coenzymes, biosynthetic intermediates, energy currency, and natural products. Therefore, due to significant biological importance and potency, nucleosides and nucleotides have fascinated chemists and biologists, and therefore an enormous number of papers related to nucleosides and nucleotides have been published worldwide. In particular, many nucleosides and nucleotides-related drugs including antisense agents have been developed and used as effective clinical therapies, clearly demonstrating that nucleosides and nucleotides are molecules with outstanding features. It is further noteworthy that the sensational recent drug sofosbuvir, which is surprisingly able to cure fatal hepatitis virus C infection, is a uracil nucleotide analogue.

Members of the Pharmaceutical Society of Japan have made significant contribution to the science related to nucleosides and nucleotides and continue to be very active in this field. Thus, in this Current Topics, Japanese researchers who have been involved in advances in nucleosides and nucleotides chemistry summarize their recent works.

In “Chemical Ligation Reactions of Oligonucleotides for Biological and Medicinal Applications,” Hiroshi Abe and Yasuaki Kimura of Nagoya University describe their RNA interference (RNAi) system, intracellular buildup RNAi (IBR-RNAi), in which RNA fragments are build up to active small interfering RNA (siRNA) in cells through a chemical ligation reaction. In this system using a phosphorothioate group and iodoacetyl group as reactive functional groups for ligation, they successfully achieved RNAi effects without inducing immune responses.

“Synthesis and Medicinal Chemistry of Muraymycins, Nucleoside Antibiotics” by Akira Katsuyama and Satoshi Ichikawa of Hokkaido University focuses on their recent main work on muraymycins, which are nucleoside antibiotic inhibitors of phospho-MurNAc-pentapeptide translocase (MraY). They summarize their synthesis of muraymycin D2 and its simplified analogues, the improved antibacterial activity exhibited and the X-ray structure of the muraymycin D2/MraY complex.

Noriko Saito-Tarashima and Noriaki Minakawa of Tokushima University contributed the chapter “Unnatural Base Pairs for Synthetic Biology.” They summarize studies of unnatural base pairs beyond standard Watson–Crick base pairs. They

have developed unnatural ring-expanded purine–pyrimidine base pairs of four non-canonical hydrogen bonds, which have shape complementarity and enhanced stacking ability. One of the base pairs may be useful for synthetic biology due to its potency in single nucleotide insertion and PCR.

In “Synthesis of 4'-Thionucleosides as Antitumor and Antiviral Agents,” Yuichi Yoshimura and his coworkers of Tohoku Medical and Pharmaceutical University describe their contentious work on the design and synthesis of a variety of 4'-thionucleoside from sugars as chiral precursors, for which they developed an efficient Pummerer-type thioglycosylation reaction. Throughout their research, they successfully identified a potent antineoplastic nucleoside, 4'-thioFAC, and several novel 4'-thionucleosides with antiherpes virus activity.

Hisao Saneyoshi and Akira Ono of Kanagawa University are interested in nucleic acid-based drug delivery to cells, which is essential for nucleic acid-based drug therapeutics. The chapter titled “Development of Protecting Groups for Prodrug-Type Oligonucleotide Medicines” outlines their recent studies related to biolabile protecting groups for phosphodiester moieties for the development of oligonucleotides to improve cellular uptake.

“Cyclic ADP-Carbocyclic-Ribose and -4-Thioribose, as Stable Mimics of Cyclic ADP-Ribose, a Ca^{2+} -Mobilizing Second Messenger” by Satoshi Shuto of Hokkaido University reviews the results of years of chemical study on cyclic ADP-ribose (cADPR), a Ca^{2+} -mobilizing second messenger, in which a general method for synthesizing cADPR-related biologically important cyclic nucleotides was developed. Using this method, the chemically and biologically stable cADPR mimics cADP-carbocyclic-ribose (cADPcR) and -4-thioribose (cADPtR) were efficiently synthesized.

The organizer sincerely appreciates the all authors for their significant contributions and is sure that this Current Topics on nucleosides and nucleotides will interest many readers of *Chem. Pharm. Bull.*

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